REVIEW
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Favipiravir: a promising investigational agent in preventing infection and progression of COVID-19

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Competing interests
The authors declare no conflicts of interest.

Abbreviations
IFN-α, interferon-alpha; CQP, chloroquine phosphate; b.i.d., twice a day; t.i.d., thrice a day; IV, intravenous; SARS-CoV-2, Severe Acute Respiratory Syndrome-Coronavirus-2; ACE-2, Angiotensin converting enzyme; RdRp, RNA-dependent RNA polymerase; Favipiravir-RMP, Favipiravir ribose-5'-monophosphate; Favipiravir-RTP, Favipiravir ribofuranosyl-5'-triphosphate; LDH, lactate dehydrogenase; ALT, alanine transaminase; AST, aspartate aminotransferase; PT, prothrombin time; µL, microliter; g/dL, gram per deciliter; IU/L, International units per liter; mg/dL, milligrams per deciliter; ng/mL, nanograms per milliliter; FEU, fibrinogen equivalent units.

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Abstract
In late Dec. 2019, a huge number of pneumonia cases caused by novel coronavirus were reported in China. 2019-nCoV pandemic has influenced on millions of people's life across the world. This novel coronavirus was identified to be similar with MERS and SARS. Therefore, researchers and academicians across the world still trying to find out vaccines, new drug molecules against SARS-CoV-2. The principle point of this review article is to explain the activity of favipiravir in preventing COVID-19. In view of constrained data available in the literature, we specify that favipiravir treatment, among all other anti-viral drugs, accompanied by oxygen inhalation therapy, maintaining fluid and electrolyte balance, and nutritional support may be helpful in fighting COVID-19.Researches were done on already approved existing anti-viral drugs for treating ebola virus, influenza virus infection and many such anti-viral agents like favipiravir, ritonavir, remdesivir, ribavirin, oseltamivir shows promising results in preventing COVID-19 infection and their clinical trials are currently undergoing in order to discover proper treatment of COVID-19. Among the aforementioned drug candidates, a broad-spectrum RNA polymerase inhibitor favipiravir, which demonstrated a promising tolerance profile and anti-viral efficacy in patients having COVID-19 manifestations.

Keywords: antiviral drugs; clinical trial; coronavirus; COVID-19; favipiravir; RNA polymerase inhibitor; SARS-CoV-2

Highlights

A novel coronavirus, 2019-nCoV, is now becoming extensive threat to public health.

Globally, various research works are done to identify drug molecules that inhibit the replication of SARS-CoV2.

Favipiravir shows encouraging results in treating COVID-19 patients during clinical trial and as a result of it many pharmaceutical companies got regulatory approval to sell this drug against coronavirus infection.

Intercontinental widespread of COVID-19

At a very recent time, a new infectious agent, recognized as a novel coronavirus (nCoV), which caused pneumonia outburst in the late Dec 2019, at Wuhan, the capital city of Hubei Province, China [1, 2]. After analysis, experts from various health protection agencies like Centers for Disease Control and Prevention (CDC) belatedly adjudge and declared that Wuhan CoV, had caused the pneumonia breakout in Wuhan city [3]. Subsequently, World Health Organization (WHO) proposed the disease name as COVID-19 and the virus responsible for widespread of COVID-19 was named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV) [2, 3]. Till 25 July, 2020 data issued by WHO revealed that, 15,581,009 cases were authenticated to be infected with novel coronavirus and 635,173 casualties occurred globally [4]. The WHOs Director-General declared the coronavirus outbreak as pandemic on March 11, 2020 [5]. Coronaviruses are a large group of viruses belongs to the subfamily Orthocoronavirinae, family Coronaviridae, and order Nidovirales [6]. The core hereditary material is encircled by an envelope which has protein spikes, that gives it crown like appearance and crown is called 'corona' in Latin language this is the way the virus gets this name [7]. It has a diameter across of roughly 120–125nm as portrayed from ongoing investigations was done by cryo-electron tomography and cryo-electron microscopy [8]. SARS-CoV-2 belongs to betacoronaviruses and shares genomic sequence and viral structure with both Middle East respiratory syndrome coronavirus (40–50% genetically similar to MERS-CoV) and severe acute respiratory syndrome coronavirus (70–80% genetically similar to SARS-CoV), which brought 349 deaths amidst 2002–03 in China [1]. There is obstinacy for safe and effective medicinal requirements for the treatment of the disease.

Potentially active drugs against SARS-CoV-2

Various attempts have been made by the scientists and researchers to discover the drugs for treating the disease. An effective approach for drug discovery is to test existing antiviral drugs [9]. More than 30 agents have been unveiled by the researchers so far which includes western medicines, naturally occurring products, and China's traditional medicines that can be potentially effective against SARS-CoV-2. A few of such representatives are being rapidly evaluated in clinical trial interpretation and exhibited earliest efficacy and safety against SARS-CoV-2. Antiviral agents included by National Health Commission (NHC) of the People's Republic of China (PRC) in the newest statement of guidelines for preventive, diagnostic and tentative treatment of COVID-19 are interferon-α (IFN-α), ribavirin, lopinavir, ritonavir, chloroquine phosphate (CQP) & arbidol [10]. Table 1 summarizes antiviral drugs that are included in the guidelines suggested by NHC of PRC.

Apart from the drugs aforementioned which have been introduced in the Guidelines; a promising inhibitory effect has shown by two experimental drugs i.e. remdesivir for Ebola virus infection treatment and favipiravir an antiviral medication used to treat influenza in Japan [9]. Notably, antiviral movement has shown by remdesivir in the treatment of SARS and MERS in creature models. As a developing helpful methodology, remdesivir was endorsed to know its treatment impact tried in gathering of patients with COVID-19 [11]. The clinical trial in regard to efficacy and safety are currently ongoing in many research and academic institutes. Favipiravir is currently being tested in 18 clinical trials for COVID-19 treatment and results from two studies have shown positive outcome. Favipiravir is a newest RNA-dependent RNA polymerase (RdRp) blocker. Along with its anti-influenza activity, favipiravir has also the capability to block the transcriptions of bunyavirales, filovirus, alphavirus, norovirus, flavivirus, arenavirus, and other single/double stranded RNA viruses [10]. Favipiravir is intracellularly reduced to favipiravir-RTP (an active phosphoribosylated form) and is discovered via. Viral RNA polymerase as a substrate, hence obstructing the RNA polymerase action. Thus, it has been seen in many literatures that favipiravir could have potential antiviral activity against SARS-CoV-2, which is a positively-sensed single-strand RNA virus. Favipiravir (also known as favilavir) the first-ever antiviral medicine is approved by the National Medical Products Administration (NMPA) of China, formerly known as China Food and Drug Administration (CFDA), to possibly treat COVID-19. Relatively, this medication was tried in the progressing clinical test being held in Shenzhen, Guangdong region, which required around 70 patients, after which it was found to be potentially compelling in COVID-19 treatment [12]. At present there is not any medication or vaccine proves to be useful for the prevention and treatment of SARS-CoV-2 said by the CDC, WHO and the FDA. Various agents are still under clinical trials and compassionate use protocol basis on limited clinical experience and in vitro activity [13–16].

Table 1 Antiviral drugs include in the guidelines (version 6) for treating COVID-19

Drug candidates	Dose	Administrative mode	Treatment period
IFN-α	5 MU or equivalent dose, b.i.d.	Inhalation route	≤ 10 days
Lopinavir/ Ritonavir	200 mg/50mg/capsule, 2 capsules each time, b.i.d.	Oral route	≤ 10 days
Arbidol	200 mg each time, t.i.d.	Oral route	≤ 10 days
Ribavirin	500 mg each time, b.i.d./t.i.d. in combination with lopinavir/ritonavir or IFN-α	IV infusion route	≤ 10 days
CQP	500 mg (300 mg orally given chloroquine) each time, 2 times a days	Oral route	≤ 10 days

Favipiravir

Introduction

A purine nucleic acid analogue, Favipiravir (T705) is an antiviral candidate account in many clinical investigations to assess the safety and potency in pneumonic persistent due to COVID-19 [17]. It selectively interferes with the RNA-dependent RNA polymerase (RdRp) which is present in influenza and many more RNA viruses. It was originally developed through chemical modulation of a pyrazine analogue by Toyama Chemical Co., Ltd. Favipiravir has shown adequate antiviral activity against distinct strains of influenza viruses (types A, B and C) which are resist to another anti-influenza drugs like neuraminidase and M2 blockers [18].

Chemical structure

Earlier, favipiravir (6-fluoro-3-hydroxypyrazine-2-carboxamide) was well known as T705, and the pyrazine-carboxamide related different mixes T-1105 and T-1106 were developed. Their structures are appeared in (Figure1). It is broad spectrum antiviral agent suggested in Japan for treatment of influenza [19].

Mechanism of action

Favipiravir is a type of pro-drug which intracellularly converted into its active metabolite favipiravir ribofuranosyl-5′-triphosphate (favipiravir-RTP) by ribosylation and phosphorylation [18]. The compound initially changes to ribose-5'-monophosphate (RMP), by interacting with hypoxanthine-guanine phosphoribosyltransferase (HGPRT), present in eukaryotic cell, further leads to favipiravir-RTP generation. Favipiravir's antiviral activity is decreased in the existence of purine nucleotides i.e. Adenosine/Guanosine triphosphate (ATP and GTP) respectively, which indicates that the viral RNA-dependent RNA polymerase (RdRp) identifies favipiravir-RTP as a pseudopurine. Favipiravir-RTP then competes with purine nucleosides and restricts the viral replication by incorporating inside the RNA of virus and therefore potentially inhibits the RdRp of RNA viruses (Figure 2). Favipiravir-RTP inhibit influenza virus RdRp with a dose of half maximal inhibitory concentration (IC50) of 0.022 mcg/ml, but the human DNA polymerases α, β, γ subunits remains unaffected at up to 100 mcg/ml [20].

A review investigation of Ebola infection patients demonstrated that, in contrast with patients who got the WHO-suggested steady treatment, the individuals who acknowledged favipiravir treatment demonstrated generally high survival ratio and longest average survival time. Genomic sequence of the nCoV-2019 confirms the virus as a single-stranded positively-sensed RNA beta-coronavirus with similar RNA-dependent RNA- polymerase gene present in MERS-CoV and SARS-CoV. Thus, considering favipiravir as a possible drug for COVID-19, however confirmed preclinical animal studies and *in vitro* studies are still not available. Clinical trials were conducted in Shenzhen, with eighty patients to assess the safety and potency of favipiravir for treating COVID-19.

Pharmacokinetics

A study was carried out in healthy volunteers of Japan which demonstrates that favipiravir reaches to maximum concentration in plasma after 2 hours when given through oral route, and quickly reduced with a short half-life period of 2–5.5 hrs. Favipiravir bound 54% to plasma proteins in humans. Favipiravir's binding percentage to HSA (human serum albumin glycoprotein) and α1-acid glycoprotein was 65.0% and 6.5% accordingly. The main drug which undergoes liver metabolism mainly by aldehyde oxidase (AO), and partially by xanthine oxidase (XO), with production of an oxidative inert metabolite T-705M1 excrete out through nephrons of kidney [20].

Drug Interactions

Drug interactions are known to occur when the pharmacological activity of a drug is amended by accompanying use of another drug or by the presence of some other substance. Most interactions are specific types of adverse drug reactions with altered efficacy of drug. Some of the few important drug interactions are shown below in Table 2.

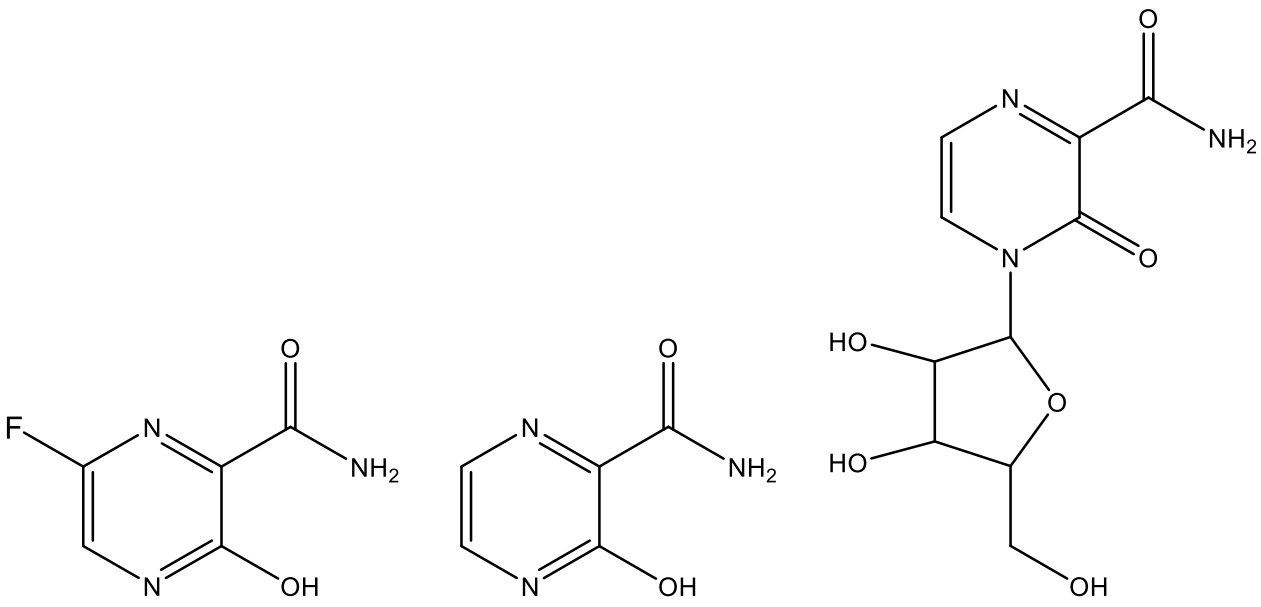

Figure 1 Structure of favipiravir (T-705), T-1105 and T-1106

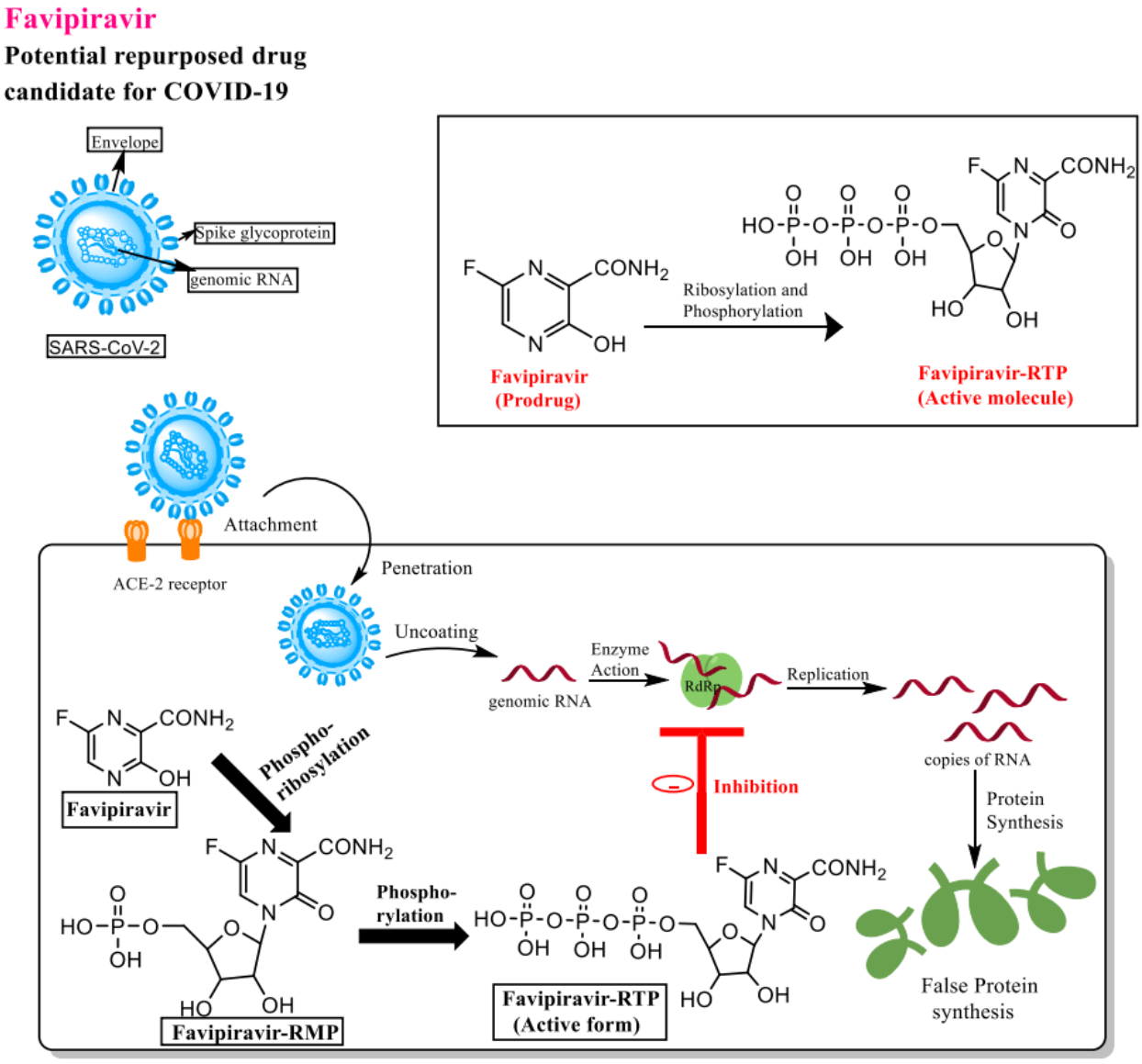

Figure 2 Schematic diagram showing mechanism of action of Favipiravir, a novel drug candidate for COVID-19

Manifestations of COVID-19

COVID-19 manifestations are non-specific and the extent of ailment may range from asymptomatic (without manifestations) to serious pneumonia and even death [21]. The clinical features of COVID-19 disease develop following an incubation period of generally 5.2 days. The duration in contrast to appearance of COVID-19 signs to demise may range following 6–41 days with an average of fourteen days. The extent of incubation depends upon patient's age and immunity which is shortened amongst patients > 70 years old in comparison to those who are below age 70 years [22]. The most predictable clinical symptoms of COVID-19 ranges from fever, cough, shortness of breath, fatigue and rarely vomiting & diarrohea [23]. COVID-19 complications include acute respiratory distress syndrome (ARDS), Liver injury, acute myocardial injury, Respiratory failure, and even multiple organ failure [24]. A study amongst ninety-nine patients reveals that approx. 17% patients establish ARDS and amongst the 11% died due to multiple organ failure. The mean duration time since first manifestations to ARDS was of eight days [25]. Affected elderly mankind with co morbidity are more prone to respiratory failure on account of serious alveolar damage [26].

Test models

Favipiravir is a substituted pyrazine carboxamide derivative and it selectively inhibits RNA-dependent RNA polymerase (RdRp) which is present in influenza A, B and C viruses. It upholds the status of treating novel or reemerging influenza virus infections in Japan in 2014 but investigation is leftover in other countries [27]

In vitro anti-influenza activity

Once Favipiravir converted intracellularly into its active form i.e. favipiravir-RTP by ribosylation and phosphorylation, that acts as a competitive substrate inhibitor of the viral RNA-dependent RNA polymerase. In vitro laboratory tests reveal that, favipiravir is active against 53 strains of influenza virus i.e. type A (H1N1, H3N2, H4N2, H7N2) and type B influenza virus. However large number of currently used antiviral like amantadine, rimantadine, oseltamivir, and zanamivir are resistant to these strains. Based on plaque reduction in Madin-Darby Canine Kidney (MDCK) cells, its 50% effective concentrations (EC50s) were in the scale of 0.014–0.55 μg/ml [18].

In vivo anti-influenza activity

Favipiravir has likewise been appeared to defend mice against deadly infection by a diversification of influenza virus strains. Favipiravir shows dose-dependent diminutions in mortality in murine models of influenza flu including infections by H_5N_1 and H_7N_9 viruses with

enlarged antiviral adequacy when joined with Neuraminidase inhibitors (NAIs). Consolidated treatment with oseltamivir and favipiravir brought about 100% survival in mice tainted with a H_5N_1 infection and stretched out the treatment window to 96hours post infection [28–30]. The results obtained from in-vitro studies reveal that consolidating favipiravir with NAIs to improve the result of extreme influenza virus infections, supplement helpful therapeutic alternatives for outbreak management [18].

Clinical trial status

Numerous clinical investigations with differing portion regimens have been led in grown-up volunteers running from age groups 18–80 years, having affirmed COVID-19. One such investigation as of late occurs at Ain Shams University Research Institute-Clinical Research Center Cairo, Egypt. Study incorporates a square randomization configuration (open mark) with approximately 100 patients with affirmed COVID-19 will be randomized among favipiravir and the standard of care treatment (rewarded by the national convention) in a 1:1 proportion.

Group 1 having 50 patients will receive the investigational drug favipiravir.

Group 2 having 50 patients will receive oseltamivir and hydroxychloroquine as the national standard of care therapy.

Outcome reveals that patients receiving favipiravir have viral clearance time and clinical improvement time of 14 days [31].

Another clinical study undergoing at Royal College of Surgeons in Ireland-Medical University of Bahrain. They did a parallel, prospective, interventional and randomized open label pilot trial involving 150 patients with COVID-19 disease. On confirmation of SARS-CoV-2 infection subjects will be randomized to hydroxychloroquine or favipiravir or standard clinical care [32].

Laboratory Diagnosis

Blood test

In the earliest phase of the disease [33], lymphocytopenia occurs with reduction of CD_4 & CD_8 cells, prothrombin time is prolonged [34], and liver enzymes, myoglobin & lactate dehydrogenase levels are raised in few patients. Troponin level also rises in few serious patients.

C-reactive protein levels and ESR (erythrocyte sedimentation rate) becomes higher in most of the patients, but procalcitonin levels remains to the normal.

D-dimer and ferritin levels elevates in case of serious patients [33]. Table 3 summarizes the laboratory abnormalities that a COVID-19 patient has to suffer along with their probable clinical significance and their normal reference values.

Plasma levels of interleukin-2 (IL-2), interleukin-10 (IL-10), Monocyte Chemo attractant Protein-1 (MCP-1), interleukin-7 (IL-7) and the tumor necrosis factor (TNF-α) are seen greater i.e. ICU patients in comparison to Non-ICU patients [34].

Table 2 Common drug interactions of favipiravir

Sr. No.	Drugs	Interactions
1.	Acyclovir	Favipiravir when given with acyclovir the excretion of acyclovir is decreased.
2.	Allopurinol	Favipiravir when given with allopurinol the excretion of allopurinol is decreased.
3.	Almotriptan	Favipiravir decreases the metabolism of almotriptan when given in combination.
4.	Alprostadil	Favipiravir when combined with Alprostadil the excretion of alprostadil can be decreased.
5.	Apixaban	Favipiravir when given with apixaban the serum concentration of apixaban is decreased.
6.	Benzyl penicillin	Favipiravir when given with benzyl penicillin in combination excretion of benzyl penicillin decreases.
7.	Captopril	Captopril excretion may be decreased when captopril is administer in combination with Favipiravir.
8.	Digoxin	Favipiravir when given in combination with digoxin decreases the excretion rate of Digoxin which raises the serum to higher levels.
9.	Ibuprofen	Favipiravir decreases the metabolism of Ibuprofen when both given combined.
10.	Omeprazole	Favipiravir decreases the metabolism of omeprazole when both given combined.
11.	Quinine	Combination of favipiravir and quinine increases the serum concentration of quinine.
12.	Ranitidine	The combination of favipiravir and ranitidine can decrease the excretion of ranitidine.
13.	Sildenafil	Combination of favipiravir and sildenafil increases the concentration of sildenafil in serum.
14.	Warfarin	Favipiravir decreases the warfarin metabolism when both given combined.

Table 3 Probable clinical significance with abnormal laboratory values seen in COVID-19 patients

Laboratory abnormalities	Probable clinical significance	Normal range
Leukocytosis	Systemic bacterial (super) infection	4,500–11,000 WBCs/μL
Neutrophilia	Systemic bacterial (super) infection	1,500–8,000 neutrophils/μL
Lymphocytopenia	Diminished immunological response against virus	1,000 and 4,800 lymphocytes/ μL
Hypoalbuminemia	Liver function impairment	3.4 to 5.4 g/dL
Increased level of LDH	Pulmonary injury and/or extensive organ damage	140–280 IU/L
Increased level of ALT	Liver damage	29 to 33 IU/L
Increased level of AST	Liver injury and/or extensive organ damage	5 to 40 IU/L
Hyperbilirubinemia	Liver injury	0.1 to 1.2 mg/dL
Elevated creatinine levels	Impaired kidney function	0.84 to 1.21 mg/dL
Elevated cardiac troponin levels	Impaired cardiac function	0 and 0.4 ng/mL
Increased level of D-dimer	Significant blood clot (thrombus) formation	500 ng/mL or less FEU
Elevated PT	Increased time for blood coagulation	11 to 13.5 secs
Increased level of procalcitonin	Systemic bacterial (super) infection	0.10–0.49 ng/mL

Specimen collection
The specimen collection for the detection of SARS-CoV2 should be taken from upper and lower respiratory sources such as throat, nasal, nasopharyngeal, sputum, and bronchial fluid. Wang et al stated that the oropharyngeal (OP) swabs (n = 398) were much used than nasopharyngeal swabs (n = 8) in China; however, the coronavirus RNA was detected only in 32% of OP swabs which was subsequently lesser than in NP swabs (63%) [35, 36]. Specimens from upper respiratory tract must be taken subsequent to onset of symptoms for sensitive analysis of human coronavirus. Exceptionally, SARS-CoV RNA constantly determined in feces 2 weeks later onset of symptoms [35]. The collected specimens should be packaged and delivered to the laboratory by maintaining cold storage chain at 2–8 ˚C.

Nucleic acid amplification tests (NAAT) for SARS-CoV2
The persons which are sensed positive for COVID-19 disease confirmed on the basis of detection of unique sequences of virus RNA by NAAT such as real-time reverse-transcription polymerase chain reaction (rRT-PCR). Chinese researchers were able to segregate a strain of the coronavirus and publish the genetic sequence so that laboratories across the world could develop polymerase chain reaction (PCR) tests independently to detect infection by SARS-CoV2.

Serological testing
In these cases, where NAAT assays give negative results and there is a strong epidemiological link to COVID-19 infection paired with serum samples could support diagnosis once verified serological tests are available.

Viral sequencing
When we develop virus whole genome, the viral sequencing method can also be used as diagnostic tool for COVID-19.

Viral culture
Virus isolation is not endorsed as a regular diagnostic tool for detection of nCoV-19 [37].

X-Ray and chest scanning
X-Ray and chest scanning reveals the presence of multiple bilateral cavitary lesions or ground glass opacities in lungs of the modest and serious inpatients [35].

WHO guidelines regarding public healthcare and social norms in workplace

Considering COVID-19, countries over the globe have sanctioned a scope of general wellbeing and accepted practices, including restrictions in movement, partial closure or fully closure of schools and organizations, isolate in explicit geographic site zones and universal travel limitations. Various nations are now trying to alter these measures as the local epidemiology of disease changes with time. As transmission power decays, a few nations will start to bit by bit re-open work environments to keep up monetary movement. This requires establishing defensive measures including physically distance maintaining, frequently hand washing, respiratory hygiene and, potentially, thermal scanning.

Guidelines
All-inclusive norms for counteracting transmission of COVID-19 that applies to all work environments and to all individuals at working environment, for example, businesses, administrators, laborers, temporary workers, clients and guests, involves the following:
Hand sanitary measures
Regular and throughout washing of hands with soap and water or hands cleaning with alcohol-based hand-rub prior to initiation of work, preceding eating, repeatedly through the working time, especially following contact with co-workers or consumers, subsequently preceding to the toilets or washrooms, after coming in contact with discharges, excretions and body liquids, after touching the possibly unsanitary belongings (gloves, clothing, masks, used tissues, waste).
Respiratory sanitary measures
Encourage people at the workplace that they have to follow respiratory sanitary measures. Assure that clinical face masks/shields and tissue paper are accessible at the working environment, for the people who manifests a runny nose or cough at work location, alongside dustbins with coverings for proper hygienic discard should be available.

Establish a methodology on how to wear a face mask or a face covering in accord with nationalized or localized instructions. In case any of employee is sick, they must not enter the workplace. If it seems that a staff member or a worker feels unhealthy when at workplace, give him a medical face mask so that they may reach to home securely.
Physical distancing norms
Establish standards with keep a distance of not less than 1 meter among individuals and maintaining a direct physical distancing among individuals (for example embracing, being touched, handshakes), keeping strictness over outside travels, line control (markings on the floor, boundaries).

Reducing frequency of people in the premises (one person only per ten square meters).

Restrict the physical assemblies or delay workplace functions that include proximate and persistent contact in between individuals, do such interactions via. Teleconferencing resources.
Minimize and manage work-regarding travels
Reduce or avoid travelling to areas with commune spread of COVID-19, provide workers with hand sanitizer for whom travelling is must, encourage workers to consent to rules from localized authority where they are wandering, in addition to give knowledge about contact authorities whom they can approach if it feels unhealthy during travels.

Employees returning back from a region where spread of COVID-19 is emerging should screen themselves for symptoms for fourteen days and keep check on their body temperature two times every day; if they feel unhealthy, they must stay at house, self-conscious, and contact medical authorities.
Standard ecological cleaning and sanitization
Washing, utilizing soap or a harmless cleansing agent, water, and mechanized activity (scrubbing, cleaning) removes soil, garbage, and different materials from surfaces. After the cleaning methodology is done, sanitization is done to inactivate (i.e. kill) microbes and different microorganisms on surfaces.

Disinfectant preparations should consistently be processed and utilized by the manufacturer's directions, including guidelines to ensure the wellbeing and safety of sterilizing laborers, utilization of individual defensive mechanism, and escaping from blending diverse chemical disinfectants.

Managers, employers, workers and their associations should synchronize with healthcare experts in the counteraction and control of COVID-19. Co-ordination among the executives and laborers and their delegates must be a fundamental component of working location-related precautionary actions and regarding the right and duties of laborers and bosses in professional health safety [38].

Conclusion

Favipiravir is a promising drug candidature for antiviral action and provides an alternate for solicitous application in COVID-19 as per its mechanism of action potentially inhibits the RdRp of RNA viruses. Genomic sequence of the nCoV-2019 reflects the virus as a single-stranded positively-sensed RNA beta-coronavirus with similar RNA-dependent RNA- polymerase gene present in MERS-CoV and SARS-CoV. Thus, considering favipiravir as a promising drug candidate for preventing infection and progression of COVID-19.

Expert opinion

As the pandemic of COVID-19 has reflected a significant challenge in therapeutic applications. Though it enhances the fatality rate of COVID-19 infected patients. The severity of health due this enhances day by day who requires mechanical ventilation. Currently, there are no therapeutics approved as a treatment option by U.S. Food and Drug Administration (FDA) for COVID-19. Current clinical management involves oxygen inhalation therapy, maintaining fluid and electrolyte balance, and nutritional support may be helpful in fighting COVID-19. Extensive research have evaluated various potential targets including, aminoquinolines (hydroxychloroquine/chloroquine), immunomodulators (steroids, anti-interleukin agents, intravenous immunoglobulin, mesenchymal stromal cells), antiviral drugs (favipiravir, remdesivir, lopinavir), antiplatelet drugs (aspirin, clopidogrel, and glycoprotein IIb/IIIa receptor antagonists) and anticoagulants (unfractionated and low molecular weight heparin, warfarin), corticosteroids (dexamethasone), angiotensin-converting enzyme inhibitors (enalapril, captopril), angiotensin receptor blockers (losartan) and nonsteroidal anti-inflammatory drugs (NSAIDs) for a co morbid condition have been studied. To overcome the hurdles in finding new discoveries of drugs researches were done on already approved existing anti-viral drugs for treating ebola virus, influenza virus infection and many such anti-viral agents like favipiravir, ritonavir, remdesivir, ribavirin, oseltamivir shows promising results in preventing COVID-19 infection and their clinical trials are currently undergoing in order to discover proper treatment of COVID-19. Among the aforementioned drug candidates, a broad-spectrum RNA polymerase inhibitor favipiravir, which demonstrated a promising tolerance profile and anti-viral efficacy in patients having COVID-19 manifestations. Favipiravir gives a substitute to humane use in COVID-19 patients depending upon its mechanism of action inhibiting virus RdRp and safety data in previous clinical studies. Till date several pharmaceutical companies got regulatory approval for manufacturing favipiravir in India namely, Glenmark Pharmaceuticals Limited, Hetero Drugs Limited, Cipla Limited, Sun Pharmaceutical Industries Limited and Dr. Reddy's Laboratories. Many vaccines trails are undergoing in various research institutes around the globe for the development of effective vaccine but till then clinical trials should help define the best strategy to treat COVID-19.

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